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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/561,487

12/19/2005

Dennis Drayna

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EXAMINER

WEGERT, SANDRA L

ART UNIT

PAPER NUMBER

1647

MAIL DATE

DELIVERY MODE

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PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	10/561,487	DRAYNA ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	SANDRA WEGERT	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 02 May 2008.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1-28, 30, 32-41, 43-48, 50 and 51 is/are pending in the application.
- 4a) Of the above claim(s) 17-19, 26-28, 30, 32-41, 45-48, 50 and 51 is/are withdrawn from consideration.
- 5) ☒ Claim(s) 1, 2, 5, 20, 21, 23, 24, 43 and 44 is/are allowed.
- 6) ☒ Claim(s) 3, 4, 6, 7, 8-16, 22, 25 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 19 December 2005 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)            | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. _____                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>8/24/06, 8/24/06</u>  | 6) <input type="checkbox"/> Other: _____                          |

**Detailed Action*****Status of Application, Amendments, and/or Claims***

Applicant's election of Invention I (claims 1-16, 20-25, 43 and 44) and the species T2R44, without traverse, in the paper of 2 May 2008, is acknowledged. Claims 17-19, 26-28, 30, 32-41, 45-48, 50 and 51 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected Invention, there being no allowable generic or linking claim. The amendment, submitted 2 May 2008, is acknowledged. Applicants amended claims 1-3, 6, 7, 15, 16, 20, 23, 26, 32, 34-36, 39, 40, 43, 47, 48, 50 and 51. Applicants had cancelled claims 29, 31, 42, 49 in a prior amendment (19 December 2005).

Claims 1-6, 20-25, 43 and 44 are under examination in the Instant Application.

**Informalities*****Specification***

The disclosure is objected to because of the following informalities:

***URL's***

The disclosure is objected to because it contains browser-executable code. This occurs, for example, on page 35, line 29, for example. All URL's should be removed from the Specification. Applicant may refer to web sites by non-executable name only. See MPEP § 608.01 (p).

Appropriate correction is required.

### **Claim Rejections/Objections**

#### **Claim Rejections - 35 USC § 112, second paragraph, indefiniteness.**

The following is a quotation of the second paragraph of 35 U.S.C. 112:

**The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter that the applicant regards as his invention.**

Claims 3, 4 and 6-16 are rejected under 35 U.S.C. 112, -second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 3 and 4 are indefinite for potentially deleting essential elements from claims from which they depend. Since the dependent claims describe an array that might contain only one of the nucleic acids listed (since they recite "at least one"), the claims do not properly depend from the independent claim. It is suggested that applicants refer to the "array of claim 2, further comprising at least one nucleic acid," or words to that effect, to overcome this rejection.

Claims 3, 4 and 8 are indefinite in that they are incomplete. The claims refer to a figure or table in the specification in which essential elements (sequences) are found (Figure 1 or Table 7).

Claims 6-16 are indefinite for referring to a "collection" of nucleic acids. It is not known precisely what is meant by this term, and it is not defined in the instant specification. It cannot be determined from the specification if "collection" encompasses an array, a population of genes, or some other grouping. In addition the term makes the

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scope of the claims inconsistent, since it is used to refer variously to groups of individual nucleic acids molecules (Claim 6, for example) as well as groups of *arrays* (claim 15, for example).

***Claim Rejections-35 USC § 112, first paragraph - enablement***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

**The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.**

Claims 22 and 25 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claims contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim 22 and 25 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated or cultured cell comprising SEQ ID NO: 188, 190, 192, 198 or 200, as well as use of the isolated cell and expression vectors, does not reasonably provide enablement for a transformed cell comprising SEQ ID NO: 188, 190, 192, 198 or 200. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The examiner has interpreted the claims as reading on isolated transformed cells, as well as on transformed cells in the context of a multicellular, transgenic organism.

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The specification of the instant application teaches that SEQ ID NO: 188, 190, 192, 198 or 200 can be expressed in transgenic animals and any technique known in the art may be used to introduce a T2R transgene into animals to produce the founder lines of transgenic animals (Specification, paragraph 0216, for example). However, there are no methods or working examples disclosed in the instant application whereby a multicellular animal with the incorporated ("knocked-in") T2R gene of SEQ ID NO: 188, 190, 192, 198 or 200 is demonstrated to express the T2R peptide. The unpredictability of the art is *very high* with regards to making transgenic animals. For example, Wang et al. (1999, Nuc. Acids Res. 27: 4609-4618; esp. pg 4617) surveyed gene expression in transgenic animals and found in each experimental animal with a single "knock-in" gene, multiple changes in genes and protein products, often many of which were unrelated to the original gene. Likewise, Kaufman et al (1999, Blood 94: 3178-3184) found transgene expression levels in their transfected animals varied from "full" (9 %) to "intermediate" to "none" due to factors such as "vector poisoning" and spontaneous structural rearrangements (pg 3180, col 1, 2<sup>nd</sup> full paragraph; pg 3182-3183). The literature teaches that the production of transgenic animals by microinjection of embryos suffers from a number of limitations, such as the extremely low frequency of integration events and the random integration of the transgene into the genome which may disrupt or interfere with critical endogenous gene expression (Wigley et al., 1994, Reprod Fert Dev 6: 585-588). The inclusion of sequences that allow for homologous recombination between the transgenic vector and the transformed cell's genome does not overcome these problems, as homologous recombination events are even rarer than random events. Therefore, in view of the extremely low frequency of both targeted and non-targeted homologous recombination

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events in microinjected embryos, it would have required undue experimentation for the skilled artisan to have made any and all transgenic non-human animals according to the instant invention. Furthermore, regarding gene targeting in embryonic stem cells, the specification does not provide guidance for identifying and isolating embryonic stem cells or for identifying other embryonic cells which are capable of contributing to the germ line of any animal. At the time of filing, Campbell et al. teaches that, "in species other than the mouse the isolation of ES cells has proved more difficult. There are reports of ES-like cell lines in a number of species...However, as yet there are not reports of any cell lines which contribute to the germ line in any species other than mouse" (Campbell et al., 1997, *Theriology* 47(1): 63-72; see pg 65, 2<sup>nd</sup> paragraph). Thus, based on the art recognized unpredictability of isolating and using embryonic stem cells or other embryonic cells from animals other than mice to produce transgenic animals, and in view of the lack of guidance provided by the specification for identifying and isolating embryonic cells which can contribute to the germ line of any non-human mammal other than the mouse, such as dogs or cows, the skilled artisan would not have had a reasonable expectation of success in generating any and all non-human transgenic animals using ES cell technology.

Due to the large quantity of experimentation necessary to generate a transgenic animal expressing the T2R protein, the lack of direction/guidance presented in the specification regarding how to introduce a T2R nucleic acid into the cells of an animal to be able produce that T2R, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art which establishes the unpredictability of making transgenic animals, and the breadth of the claims which fail to

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recite any cell type limitations, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope. (Please note that this issue could be overcome by amending the claim to recite, for example, “An isolated transformed cell...”).

**Conclusion:** Claims 3, 4, 6, 7, 8-16, 22, 25 are rejected for the reasons recited above.

Claims 1, 2, 5, 20, 21, 23, 24, 43 and 44 are allowable.

#### **Advisory information**

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sandra Wegert whose telephone number is (571) 272-0895. The examiner can normally be reached Monday - Friday from 9:00 AM to 5:00 PM (Eastern Time).

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Manjunath Rao, can be reached at (571) 272-0939.

The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO



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Customer Service Representative or access to the automated information system, call 800-786-9199 (in USA or CANADA) or 571-272-1000.

/SLW/

22 July 2008

/Elizabeth C. Kemmerer/  
Primary Examiner, Art Unit 1646